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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

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EDITORIAL

FIRST THINGS FIRST

IN this issue we have published an article on the need for better public relations in pharmacy. In this article are given figures concerning the per capita expenditures of Americans for such items as alcoholic beverages ($55), tobacco ($32) and drugs, including sundries ($10). These figures in themselves are enough to shatter the illusions held by many laymen concerning the high cost of drugs and every pharmacist should be prepared to quote them. As a corollary we might cite the national disgrace in the field of education where again our outlay for alcoholic beverages or tobacco exceeds what we spend for education, both public and private, from the kindergarten to post-doctoral research.

It is difficult for many to accept the truth of these figures for what they portray is not a pretty picture. Neither does it speak well for the future of our country. The ugly truth is that we as Americans have the unfortunate habit of failing to put first things first in the allocation of our earnings and resources.

Neither alcoholic beverages nor tobacco are really essential to man's welfare and happiness, and a good case can be made against both as causes of illness, disability and early death. While to the person addicted to either they seem indispensable, the individual using neither is undoubtedly better off. No one, however, objects to the cost of these products, for they are avidly sought as a source of selfish pleasure sometimes bordering on the extreme.

The cost of drugs, however, is another matter. No one wants to be sick in the first place and what it costs is painful even though the funds are readily available. Rather than consider the awful alternative of doing without them, it is easier to impugn the pharmacist and the physician as avaricious and greedy and to suggest that someone should investigate their nefarious business of exploiting the consumer.

Public attitude toward education is possibly of even greater potential danger. While everyone gives lip-service to the value of education few are willing to pay what good education costs. The situation in our public schools is chaotic. The shortage of teachers

grows and grows with little prospect of a reversal. Teachers' salaries have not kept abreast of the rise in cost of living or industry wages. To make things worse, teachers are often investigated or otherwise hounded until the outlook for the teacher is a drab, underpaid and underprivileged existence. Thousands have left the teaching field under economic pressure or the demands made by the need of greater self-respect. Many of our public schools have been forced to adopt a morning and an afternoon shift to accommodate the children. Thus we neglect our greatest national resource, our children.

Our colleges will soon feel the impact of these children as they reach college age, and many institutions are none too well prepared. How many will manage to maintain their educational service is a question.

The underlying cause of all of this is the failure of the American people to believe wholeheartedly in, and insist on, proper financial support for our schools. We are willing to spend billions on armaments, hundreds of millions on alcohol and tobacco, but our schools are given only grudgingly and hesistatingly. We seem to feel that some means should be available to educate our children without it costing much.

Pharmacists in their public relations work should emphasize this theme of putting first things first. We cannot afford not to take care of health needs and education above all else. A sound mind in a sound body should be the ultimate goal and aim of all. Even in our international relations this is a matter of concern. We pride ourselves in our superiority over Russia but this is an advantage which may not be permanent. Education is placed very high in the Russian schedule of priorities and in this they show superior judgment. We are now superior to these people in many ways but it is an advantage which may not always be ours. Much as we dislike saying it, they are facing certain problems which we choose to ignore.

L. F. Tice

MODERN CONCEPTS OF ANTIBIOTIC THERAPY*

By Martin Barr**

WE are all aware of the great number of antibiotics which have been developed since the work of Fleming, Florey, Chain, and others led to the discovery and use of penicillin. This has led to the necessity of most careful thought by the physician as to what antibiotic is of choice for a specific infection.

When a physician selects an antibiotic for use, he has the following objectives in mind:

(1) To select the antibiotic or combination of antibiotics most likely to terminate the infection in question;

(2) To use the route of administration and dosage most likely to be effective;

(3) To avoid harmful side reactions; and

(4) To select the most economical program of therapy.

Each new antibiotic that is introduced adds some new feature to the armamentarium of the physician trying to cope with the infectious processes. Each may also add some new hazard (side reactions). In this short talk, I cannot hope to cover adequately the whole field of antibiotics: therefore, I shall summarize the chemistry and the activities of the antibiotics in as short a form as possible and discuss in addition other factors of importance in the selection of antibiotics for use.

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* Presented at the Annual Convention of the National Pharmaceutical Association, August 3, 1954, Philadephia, Pa.

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General

The structural formulas of some of the antibiotics are illustrated in Figure I. The spectra of the antibiotics is summarized in Table I.

TABLE I.—ANTIBIOTICS SPECTRA

PENICILLIN

1. Gram-positive bacteria
2. A few gram-negative bacteria
3. A few spirochetes
4. A few actinomycetes
5. A few large viruses

TETRACYCLINE (ACHROMYCIN, TETRACYN)
CHLOROTETRACYCLINE (AUREOMYCIN)
OXYTETRACYCLINE (TERRAMYCIN)
CHLORAMPHENICOL (CHLOROMYCETIN)

1. Most gram-positive bacteria
2. Most gram-negative bacteria
3. Most rickettsias
4. Most spirochetes
5. Some large viruses
6. A few protozoa

BACITRACIN

1. Gram-positive bacteria
2. A few gram-negative bacteria
3. A few spirochetes
4. A few protozoa

NEOMYCIN

1. Most gram-positive bacteria
2. Most gram-negative bacteria
3. Most actinomycetes
4. A few yeasts

STREPTOMYCIN and DIHYDROSTREPTOMYCIN

1. Many gram-positive bacteria
2. Most gram-negative bacteria
3. A few spirochetes

ERYTHROMYCIN and CARBOMYCIN

1. Most gram-positive bacteria
2. Some of the gram-negative bacteria
3. Most rickettsias
4. Some spirochetes
5. Some large viruses
6. A few protozoa

POLYMIXIN

1. Gram negative bacteria

TYROTHRICIN

1. Gram-positive bacteria
2. A few gram-negative bacteria
3. A few spirochetes

FUMAGILLIN

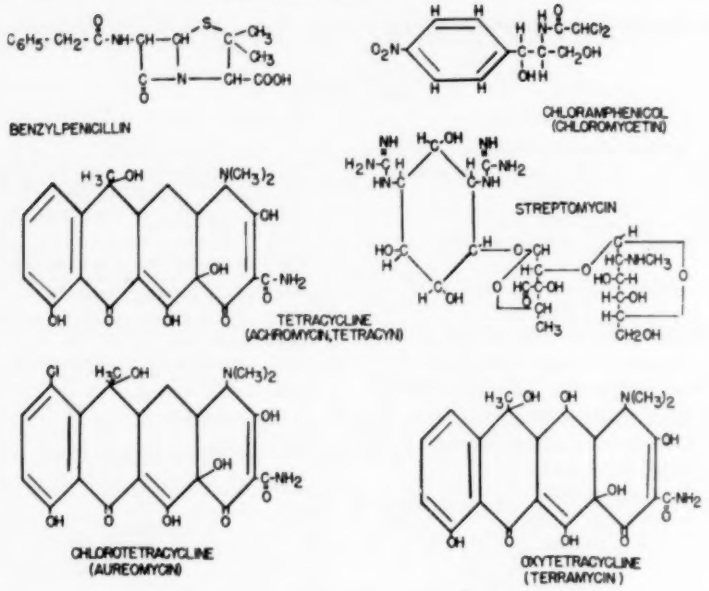
1. Amebicide

VIOMYCIN

1. Anti-tubercular

Penicillin remains the most widely used of the antibiotics. Considering efficacy, safety, and cost, pencillin is still the antibiotic of choice for most susceptible infections. The introduction of the repository forms of pencillin has also added to its usefulness as effective blood levels of this drug are able to be maintained for long periods of time. The use of topical penicillin, however, is being discouraged because of its allergenicity and rapid inactivation by penicillinase in mixed infections.

FIG I: STRUCTURAL FORMULAS OF FIVE COMMONLY USED ANTIBIOTICS



Changes in our knowledge of the usefulness and limitations of streptomycin and dihydrostreptomycin have greatly modified their use. This antibiotic has maintained its role as a tuberculostatic drug. The combination of streptomycin with other drugs such as para-aminosalicylic acid, sulfones, or nicotinic acid derivatives has reduced the hazard of 8th nerve damage. Streptomycin finds considerable use in the treatment of infections due to Pseudomonas, Staphylococcus, colon bacillus, Pasteurella (tularemia), Donovania (granuloma inguinale), Brucella, Hemophilus influenzae, and ducreyi (chancroid).

Tetracycline, chlorotetracycline, oxytetracycline, and chloramphenicol are quite similar in their antibiotic ranges. They are often used advantageously in penicillin—and/or streptomycin—refractory infections of unknown etiology. Chloramphenicol is especialy effective in the treatment of typhoid fever.

Erythromycin and carbomycin are recent additions to the antibiotic armamentarium. They are used very often in treating infections which are caused by organisms which have developed resistance to penicillin and also in patients where sensitivity to penicillin has been acquired.

There is increasing interest in the poorly absorbed antibiotics such as bacitracin, neomycin, and polymixin. These antibiotics are limited in systemic use because of toxicity when injected parenterally but, despite this limitation, they have proven lifesaving when given parenterally in the short courses required to control otherwise refractory infections. These antibiotics do not produce systemic toxicity when used topically or orally (oral use is essentially an enteric topical application). Polymixin is most useful in Pseudomonas, E. coli, and Shigella injections. Bacitracin has an antibiotic range roughly paralleling that of penicillin but, unlike penicillin, is not inactivated by mixed injections. Neomycin is very effective against nearly all pyogenic infections of the skin, mucous membranes, and eyes since it has a very wide range of activity against both gram-positive and gram-negative organisms and rarely induces hypersensitivity. Although the broad spectrum antibiotics are also effective topically, drugs which are not generally used systemically are preferred for topical or oral use because there is little danger of sensitization to their later parenteral use.

Fumagillin is an antibiotic which finds use specifically in the treatment of amebiasis. Viomycin has proved of value in the treatment of tuberculosis. Tyrothricin is not indicated in systemic therapy although it has a spectrum similar to penicillin because of its hemolytic action. Therefore, the clinical application has been limited to topical use and certain mucous membrane infections.

Mixed Antibiotic Therapy

Because of limitations in the spectrum of the individual antibiotics, there has been a growing trend toward the joint use of two or more antibiotics in treating many infections. This practice is referred to as mixed antibiotic, polyantibiotic, or multiple antibiotic therapy.

There are various reasons for the use of mixed antibiotic therapy. Often, there is a mixed infection caused by different type organisms which are not susceptible to one antibiotic alone. There are certain

infections, such as tuberculosis, in which streptomycin may be effective initially but in which resistant strains may emerge. A second agent added to the therapeutic attack may suppress these resistant strains. The difference in penetrability of antibacterial agents to various infection sites is another important consideration. For instance, in meningococcemia or pneumococcemia, penicillin may be the most effective agent in controlling bacterial multiplication but, when the meninges are invaded by the same organisms, the addition of a sulfonamide may be desirable because these drugs enter the cerebrospinal fluid more readily.

Another reason for mixed antibiotic therapy is the production of synergism between antibiotics used simultaneously, resulting in an antibacterial effect greater than the anticipated simple additive effect. At the same time, there is also a possibility of antagonism between mixed antibiotics which would prove detrimental in therapy. Jawetz and Gunnison (1) have summarized the synergistic, additive, and antagonistic actions of antibiotics. This appears in Table II.

In general, it is advisable to avoid combinations of antibiotics when one alone is effective and to use only combinations that have proved to be efficacious against clinical injections. Some examples of mixed antibiotic chemotherapy are listed in Table III (2).

Adverse Effects of Antibiotics

Practically all of the antibiotics in use today are capable of producing toxic effects. We are familiar with the increasing number of individuals becoming sensitive to penicillin. Streptomycin and dihydrostreptomycin both are toxic for the 8th nerve. Preparations containing mixtures of both agents are available commercially and are allegedly less toxic because of the smaller individual doses required. The broad spectrum antibiotics produce unpleasant side effects in many patients such as nausea, vomiting, diarrhea, and rectal burning. Long-continued administration may lead to the overgrowth of resistant staphylococci in the intestinal tract as well as fungi such as *Cryptococcus, Aspergillus,* and *Monilia.* Severe diseases and death have been produced by these organisms in some patients. Chloramphenicol, when used systemically, is potentially a dangerous drug, capable of serious hematologic depression, and must be used with calculated risk. It is usually recommended when infection threatens life, when the organism is of known sensitivity, and when other antibiotics have been

TABLE II

Synergistic, Additive and Antagonistic Actions of Antibiotics

Narrow Spectrum		Broad Spectrum	
Bacitracin	Pairs composed of any two:		Pairs composed of any two:
Neomycin	1. Frequently synergistic	Aureomycin	1. Seldom synergistic
Penicillin	2. Sometimes additive	Chloramphenicol	2. Sometimes additive
Streptomycin	3. Seldom antagonistic	Terramycin	3. Seldom antagonistic
Action of any single member of this group against a sensitive organism may be antagonized by Aureomycin, Chloramphenicol, or Terramycin.		Action of any single member of this group usually not impeded by addition of narrow-spectrum antibiotic. If organism is resistant to narrow-spectrum drug but can be inhibited by high concentration of it, that narrow-spectrum drug may synergize action of any one of the above group.	

All of above statement subject to the following provisions:

1. For synergism to occur, each member of the antibiotic pair must be capable of inhibiting the specific micro-organism independently, although inhibitory concentration sometimes may be above clinically practicable levels.

2. Synergistic, additive, or antagonistic action of an antibiotic pair against a given organism is not assurance of similar action against another organism. The effect must be determined separately for each organism.

3. Synergistic or additive action of a pair of antibiotics against a given micro-organism in vitro is no guarantee that the same effect will occur in vivo.

4. The effect of a given pair of antibiotics on a given species of micro-organism may be synergistic, additive, or antagonistic, depending on the relative concentration of the two drugs and sometimes upon the sequence of administration.

TABLE III

SOME EXAMPLES OF MIXED ANTIBIOTIC CHEMOTHERAPY

Code: A-Aureomycin; B-Bacitracin; C-Chloramphenicol; N-Neomycin; P-Penicillin; PO-Polymyxin; S-Streptomycin or Dihydrostreptomycin; SU-Appropriate Sulfonamide; T-Terramycin; TY-Tyrothricin

Infectious Agent or Clinical Symptom	Combination Reported Effective
Actinomycosis	P + SU; P + potassium iodide
Amebiasis (Endamoeba histolytica)	T + fumagillin
Brucellosis	S + SU; A + S; T + SU; T+ C
Cervicitis, chronic, and cervical erosion	B + P
Colitis and chronic diarrhea of bacteriologic etiology	B + PO + S
Cryptococcomycosis	P + SU
Empyema	P + SU
Endocarditis, bacterial, subacute	P + S; B + P
Enteric fevers (Salmonellosis)	S + SU
Erysipeloid (caused by Erysipelothrix erysipeloides)	P + S
Gas gangrene	P + SU
Infected root canals in pulpless teeth	B + P + S
Klebsiella pneumoniae	B + P; P + S
Ludwig's angina	P + SU
Lung abscesses	P + SU; P + T
Lymphogranuloma venereum	P + S
Meningitis (due to Hemophilus influenzae)	S + SU; A + SU; T + SU
Meningococcemia, fulminating	P + SU
Osteomyelitis, chronic (Staph. aureus)	B + P
Peritonitis	P + SU
Pertussis	P + SU; P + PO
Pneumonia, pneumococcal	P + SU
Pyelonephritis (Ps. aeruginosa)	A + S
Pyogenic dermatoses	B + Ty (topical)
Salmonella typhosa	C + T
Sinorespiratory infections and sinusitis (some forms)	B + P; P + SU
Staphylococcus aureus suppurative processes and other infections	C + S; S + T; B + N; B + C; A + B; B + T; C + N; A + N; N + T; B + Ty (topical only)
Streptococcus sp., enterococcic group (infections of blood stream; subacute bacterial endocarditis)	P + S
Streptococcus sp., pyogenic group (infections of blood stream)	P + S
Streptococcus sp., viridans group (oral abscesses and subacute bacterial endocarditis)	P + S; B + P
Syphilis	P + bismuth
Urethritis, nonspecific (some forms)	P + SU

found to be ineffective. Polymixin and neomycin have both shown slight neurotoxic and nephrotoxic effects in individuals and bacitracin has been responsible for some nephrotoxicities.

Resistance to Antibiotics

The emergence of strains of organisms that are resistant to one or more antibiotics and which may perpetuate themselves in the human population is a cause of concern to clinicians and research workers. For example, in 1946, when penicillin first came into general use, 90 per cent of the population of staphylococci cultured from the ear, the nose, or the throat of hospital patients were inhibited by 2 units or less of penicillin per ml. *in vitro* but, in 1949, after three years of the widespread use of penicillin, only 50 per cent were sensitive to that concentration and about 166 units per ml. were required to inhibit 90 per cent of populations newly isolated from hospital admissions.

Organism resistance has come about principally as the result of the unwise choice of an antibiotic or its misuse. The development of resistance may be minimized by using adequate therapeutic doses of an antibiotic when indicated, discontinuing any antibiotic that may not prove effective within a few days, avoiding prolonged uninterrupted prophylaxis with antibiotics, and by making bacteriological diagnosis and using sensitivity tests where possible in all doubtful cases.

It has been observed that a pathogen which has become resistant to one antibiotic has also acquired increased resistance to others and that shifting to another antibiotic fails to arrest the disease. For the purpose of explaining cross-resistance, let us divide the antibiotics into two groups. Group I, the narrow-spectrum antibiotics, includes bacitracin, polymixin, penicillin, streptomycin, and tyrothricin. Group II, the broad-spectrum antibiotics, includes chloramphenicol and the tetracycline group of antibiotics.

Resistance to one member of Group II entails some resistance to the other members of this group. The acquisition of resistance to an antibiotic in Group I may or may not be accompanied by increased resistance to others in the same group but is not often associated with increased resistance to a Group II drug. Similarly, an organism which has become more resistant to the broad-spectrum antibiotics usually manifests comparatively little—if any—increase in resistance to the narrow-spectrum drugs. Often, there appears to be an inverse

relationship between drugs of the two groups. Organisms that acquire resistance to one or more of the Group II antibiotics frequently become more sensitive to antibiotics from Group I and vice versa.

Erythromycin and carbomycin appear to be intermediate between Group I and Group II antibiotics with respect to their effects on emergence of resistant strains of organisms but seem to resemble the narrow-spectrum group more than the broad-spectrum group. Resistance develops slowly among sensitive strains exposed to erythromycin or to carbomycin. There is pronounced cross-resistance between erythromycin and carbomycin but relatively little between these antibiotics and the narrow-spectrum or broad-spectrum group.

Conclusion

An attempt has been made to discuss in a brief manner the usefulness of the practical antibiotics. The advantages and disadvantages of mixed antibiotic therapy has been mentioned. The hazards present in the administration of the antibiotics have been pointed out.

The ideal antibiotic is one whose antibacterial spectrum would be wider than any of those so far introduced and whose adverse properties would be so mild as to make it absolutely safe for administration by all routes. No such antibiotic is available. Until such antibiotics are discovered, the antibiotics must be used with intelligence so that they will produce the maximum therapeutic effect compatible with safety.

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ARE "QUATS" FUNGICIDAL?

By Emil G. Klarmann and Eleanore S. Wright *

Introduction

OVER a period of the past several years, there occurred an increasing accumulation of arguments in favor of a revision of the earlier ideas as to the microbicidal action of quaternary ammonium compounds. These original ideas were derived from the experimental data of a number of early investigators who had attributed to the "quats" a considerably greater bactericidal and fungicidal potency than warranted in the light of more recent findings. This discrepancy between the earlier and the later data is due to several factors; chief among them is the failure on the part of the earlier researchers to recognize certain characteristic peculiarities of the "quats", which should have called for a modification of the bacteriological testing methods employed so as to take care of these peculiarities. Since the latter subject has been discussed in several of our preceding publications there appears to be no need to enlarge upon it here. Nor is it necessary to enumerate all of those older publications which, in our opinion, call for a recheck of their experimental results as well as a reconsideration of the conclusions based thereon, in order to bring them into conformity with the more recent findings obtained by means of more applicable testing techniques. Among others, the data reported by Dunn (1), and Rawlins, Sweet and Joslyn (2) would justify such a critical review since they have been, and still are being used variously to support the claims made on behalf of different types of quats which are deemed to be in need of revision, at least in their quantitative aspects.

Although several recent publications have been helpful in placing the antibacterial action of the quats in a more proper perspective (3-5), no such attempt appears to have been made to date with respect to their antifungal properties. The several older papers referred to above attribute a rather marked fungicidal potency to the quats. Thus Dunn reports phenol coefficient values ranging up to 120 at 20° C.,

* Plaut Research Laboratory, Lehn & Fink Products Corporation, Bloomfield, N. J.

and 280 at 37° C. for benzalkonium chloride against *Trichophyton interdigitale,* one of several test fungi employed (recalculated from figures actually obtained with a 1:1000 tincture). Rawlins, Sweet and Joslyn claim a marked fungicidal efficiency for benzalkonium chloride acting in the form of a 1:1000 solution (or weaker) upon three pathogenic fungi (including *Trichophyton interdigitale*) at 30° C. for 5 minutes. Claims for fungicidal action of several quats are being advanced also in promotional literature published on their behalf; thus benzalkonium chloride is said to be fungicidal for *Trichophyton interdigitale* in a dilution of 1:1000 (in 4 minutes), and benzethonium chloride is recommended for use in a dilution of 1:750 against the organism of athlete's foot. Such examples could be multiplied almost at will.

Perhaps it should be stressed at this point that the problem of the fungicidal action of quats is of more than academic interest as they are being used, among other things, for the disinfection of appliances in barber and beauty shops where the prevention of fungus infection should be a matter of primary concern. Moreover, quats are being supplied as general disinfectants against specifications in which fungicidal potency is expressly demanded as an aid in reducing the risk of infection (particularly of the feet) from surfaces contaminated with pathogenic fungi.

Adaptation of the "Semi-Micro" Method to the Testing of Fungicides

As has been shown by us before, the basic principle underlying the "Semi-Micro" method (6-8) is suited to controlling two of the most important factors which interfere with the determination of the bactericidal action of quats by regular "phenol coefficient" methods, viz. 1) their marked bacteriostatic action which beclouds their true bactericidal potency, and 2) their tendency to cause bacteria to clump or to mass against the walls of the medication tube which introduces a sampling error by preventing the transfer of a representative inoculum from the medication mixture into the subculture. Under the test conditions of the "Semi-Micro" method both these interfering factors are taken care of. This procedure calls for subculturing the entire medication mixture (consisting of diluted disinfectant plus test organisms), followed by dilution, at the end of the medication period, with nutrient broth which contains a suitable antidote; the latter step

halts the action of the antibacterial agent and, at the same time, neutralizes its bacteriostatic function. As applied to the evaluation of the bactericidal potency of disinfectants and antiseptics, the "Semi-Micro" method calls for the use of 0.05 ml. of a bacterial (broth) culture and of 0.5 ml. of diluted antibacterial agent (representing one tenth of the respective quantities required by the A. O. A. C. "phenol coefficient" technique). As a rule, Bacto-Oxgall has been employed by us successfully as the neutralizing antidote. The medication time is 10 minutes unless required otherwise, and the action of the disinfectant is stopped by the addition of 20 ml. of the diluent medium described above.

The original A. O. A. C. method of testing fungicides applies to water soluble or miscible fungicides recommended for use on inanimate articles, with the objective of destroying the pathogenic fungi capable of causing infection in man or animals. (It is not intended to answer questions as to the therapeutic efficiency of fungicides prescribed for the treatment of pathological skin conditions caused by fungi.) Since the principle of the "Semi-Micro" method served us well in helping to distinguish bactericidal from bacteriostatic action, especially in the case of quaternary ammonium compounds, it seemed logical to adopt it in developing a testing procedure for quats designed to clarify their antifungal performance, *viz.*, by deciding whether or not the dilutions represented as "fungicidal" by some investigators were in fact fungicidal within the meaning of this term.

It was found at an early stage of the work that the quats are indeed possessed of a very marked fungistatic but a low fungicidal capacity. Accordingly, in adapting the "Semi-Micro" technique the ratio of the diluent to medication mixture had to be shifted greatly in favor of the former for the sake of more effective neutralization of the fungistatic effect. This was done by reducing the proportions to 0.1 ml. of diluted disinfectant and 0.01 ml. of fungus spore suspension. The amount of the diluent medium (plus antidote) was left unchanged, i.e., 20 ml.; owing to the greater ratio of diluent to medication mixture the former's effectiveness in halting the reaction and in neutralizing fungistasis must have been stepped up appreciably. Repeated control tests with pure phenol indicate that operating with the smaller quantities of fungus spore suspension and disinfectant solution nevertheless can yield entirely reproducible results.

In all cases, the reaction time was 10 minutes at room temperature (20° C.), and the incubation period was 2 weeks at 28° C.

Test Results

The following Table I compares the results with respect to two test organisms, *Trichophyton interdigitale* (640) and *Trichophyton rubrum* (ATC 10218), as obtained by means of three testing methods, viz. respectively, the A. O. A. C. method modified as recommended by its authors for products suspected of a fungistatic character, the A. O. A. C. method modified by the use of Letheen broth in the subculture tubes for more effective neutralization of any inhibitory concentration of the active ingredient transferred into them, and the "Semi-Micro" method, adapted as described above for a more effective elimination of fungistasis.

The data given in the table, as obtained by the first and the second method, do not indicate the great variability of results which is encountered regularly in testing quats for their antifungal performance; and this in spite of the fact that in the case of both methods due consideration is being given to the need of controlling fungistasis. To this extent, therefore, the data obtained by these two methods must be regarded as approximate. In the case of the third, the "Semi-Micro" method, fungistasis appears to have been eliminated in all instances but one; constant figures have been obtained by this method, as a rule.

It is quite evident that the so-called "fungicidal" dilutions of the quats tested as obtained by means of the A. O. A. C. method (first series) must be fictitious in spite of the employment of a modifying expedient intended to control their fungistasis. More effective methods of suppressing fungistasis indicate the virtual absence of any true fungicidal quality (second and third series). In fact, quat solutions as strong as 10 percent did not produce any truly fungicidal performance with respect to *Trichophyton interdigitale* when practically complete elimination of fungistasis was achieved either by the use of Letheen broth in the transfer tubes or by employing the "Semi-Micro" method. It is noteworthy that with pure phenol comparable fungicidal results were obtained by all three methods.

Parenthetically speaking, it is somewhat surprising that the "A. O. A. C. Fungicidal Test—First Action" does not suggest the use of "Letheen" broth in the case of quats, in view of the fact that "Letheen" broth is recommended in another A. O. A. C. procedure, viz. the "A. O. A. C. Phenol Coefficient Method—Official" when applied to "products containing cationic surface active materials".

TABLE I

	Original A. O. A. C. Method (With Subtransfer)		Modified A. O. A. C. Method (Without Subtransfer, Letheen Broth)		K-W "Semi-Micro" Method (Adapted to Fungicide Testing)	
	T. interdigitale	T. rubrum	T. interdigitale	T. rubrum	T. interdigitale	T. rubrum
Benzalkonium chloride	1:100	1:200	Not in 1:10	1:20	Not in 1:10	Not in 1:10
Benzethonium chloride	1:80	1:1000	Not in 1:10	1:1000	Not in 1:10	Not in 1:10
Cetyl pyridinium chloride	1:800	1:100	Not in 1:10	Not in 1:10	Not in 1:10	Not in 1:10
N-(lauroyl colaminoformyl methyl) pyridinium chloride	1:20	1:100	Not in 1:10	Not in 1:10	Not in 1:10	Not in 1:10
Alkylated (C_9C_{15}) tolyl methyl trimethyl ammonium chlorides	1:2000	1:4000	Not in 1:10	1:6000	Not in 1:10	Not in 1:10
Lauryl isoquinolinium bromide	1:2000	1:1200	Not in 1: 5	1:40*	Not in 1: 5	1:40*
N-soya-N-ethyl morpholinium ethosulfate	1:200	1:100	Not in 1:10	Not in 1:10	Not in 1:10	Not in 1:10
Phenol (control)	1:45 to 1:60	1:80	1:60	1:80	1:45 to 1:60	1:70

* fungistasis

Experimental Part

Method I. The A. O. A. C. method used is that given in the Official Methods of Analysis of the Association of Official Agricultural Chemists, 7th ed. (1950), p. 91. The suspensions of 10 day old cultures were adjusted to contain 5 million spores per ml. One-half ml. of spore suspension was added to 5 ml. of diluted disinfectant at 20° C. At the end of 10 minutes a 4 mm. loopful of suspension was withdrawn, touched to the surface of a tube of dextrose broth and immediately immersed in a second tube of dextrose broth. (This precautionary modification is recommended by the A. O. A. C. method as a means of eliminating fungistasis; its effectiveness appears to be highly questionable.) All tubes were incubated for 2 weeks at 28° C.

Method II. This is the same as Method I except that 0.7 gm. of lecithin ("Azolectin") and 5 gm. of sorbitan monooleate ("Tween 80") was added to each liter of subculture broth. When transferring from the medication mixture the loop was immersed in the broth immediately, followed by shaking. No second tube of broth was used (as in Method I).

Method III. The principle of the "Semi-Micro" method of Klarmann and Wright was adapted with the particular aim to eliminate the factor of fungistasis. To this end, only 0.1 ml. of diluted disinfectant and 0.01 ml. of spore suspension is used. The latter is placed at the bottom of a 22 × 150 mm. test tube and held in a water bath of 20° C. whereupon the diluted disinfectant is added and mixed with the spore suspension. At the end of 10 minutes, 20 ml. of dextrose broth containing 2 percent of "Bacto-Oxgall" is added. Results are read after 2 weeks' incubation at 28° C.

Conclusion and Summary

The "A. O. A. C. Fungicidal Test" is not satisfactory for determining the fungicidal potency of quaternary ammonium germicides because it makes but an inadequate provision for the control of the pronounced fungistasis of this class of compounds which tends to obscure any fungicidal action. The addition to the subculture broth of lecithin and sorbitan monooleate (as recommended originally for the control of bacteriostasis in the "A. O. A. C. Phenol Coefficient Method" for testing quats with *Salmonella typhosa* and *Micrococcus pyog.* var. *aureus*) suppresses most of the fungistasis with the result

that the quats are revealed to be practically devoid of fungicidal capacity in any practical dilution with respect to such important microorganisms as *Trichophyton interdigitale* and *Trichophyton rubrum*.

This contention is confirmed by the results obtained with an adaptation of the authors' "Semi-Micro" method to fungicide testing; incidentally, the latter results are substantially free from irregularities owing to effective suppression of the random sampling error which constitutes one of the pragmatic features of this method.

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THE NEED FOR BETTER PUBLIC RELATIONS IN PHARMACY *

By Robert E. Abrams **

IT seems that in order for one to address a pharmaceutical convention on anything but a scientific subject, a speaker must be both a diagnostician and an able prescriber, for almost every program carries titles indicating diagnosis, treatment and prognosis for the ills of pharmacy. Actually, if pharmacy was as sick as some would have us believe, I am certain it would have died by this time. There is no question that the profession of pharmacy is going through an era of change and, as with any progress, there is a reluctance and a difficulty to comprehend all its many manifestations. Pharmacy will grow and advance as long as pharmacists want it to, but it is important that this desire be backed up with action as well as words. What pharmacy needs most at the present time is the good will and support of the general public. Pharmacy needs and deserves public confidence, public acceptance and public respect. This can only be accomplished by the deeds and conduct of individual practicing pharmacists and not by flowery speeches.

Without the respect and confidence of our patients or customers, how can pharmacy advance? We are familiar with the biblical quotation, "What does it profit a man if he gain the whole world and suffer the loss of his own soul?" The soul of our profession is the esteem which the public and our sister professions hold for pharmacy. Without this soul, pharmacy can not continue to progress.

Public relations is every pharmacists' responsibility; his own individual responsibility, and like charity, it begins at home. Since we are banded together in a profession, we are our Brother's Keeper. . . . Anything accomplished, whether satisfactorily or otherwise, reflects back on all of us and, unfortunately, we are judged, not by the best, but by the worst, as far as public relations are concerned. There is no question that public relations-wise pharmacy has failed miserably to convey the story of the many contributions that pharmacy has made in keeping the American Public healthy.

We can single out many reasons for this failure to convey the story of pharmacy to the public. The manufacturer who is in a posi-

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tion to provide such a program for pharmacy has as yet not come forth with anything of definite value; the pharmaceutical organizations also have not developed the type of unified coordinated program needed, although the American College of Apothecaries have made the first attempt to offer such a program and this has met with a great deal of success. However, the primary failure must be attributed to the individual retail pharmacist. For in the main, he has not seen fit, either through ignorance or indifference to present the type of appearance, thinking and effort that will inspire an appreciation by the public.

Pharmacy has the unique distinction of being a profession that is not entirely a profession. There is little that ties pharmacy together and with this lack of cohesiveness pharmacy has lost a great deal. Laws are passed, decisions are made, vitally affecting pharmacy; yet rarely is pharmacy consulted. We frequently speak of the prescription department being the "heart" of the drugstore. It is frequently said that prescriptions are our monopoly and can not be taken from us. However, how strong is this hold? It is but a thin printed line, the prescription legend on the label. Remove the legend and in certain states these products can be sold by anyone. In order for this heart to survive and beat, it must be constantly nourished by a professional atmosphere. Until we can convince the public, not the legislators, the newspapers or the courts that pharmacy is a profession and exercises professional supervision in the sale of drug products, we can never hope to derive the professional respect rightfully deserving to pharmacy.

Pharmacy needs better public support, more confidence, and a better understanding. Pharmacy must prove to the public that it is a very much needed profession. Pharmacy has to convince the public that it is to their personal health and welfare to patronize the drug store.

Pharmacists are told to follow supermarket techniques and many have adopted this method to combat supermarket competition. Pharmacy is not geared for such competition and when they accept this method they become the imitator instead of the leader. By this, I do not mean we should refuse to adopt new merchandising techniques. By all means utilize these where they apply, but do not lose sight of the fact that pharmacy is a profession and as such the public is entitled to professional service, appearance and supervision when it comes into our pharmacies.

Pharmacy, as a profession, and industry has a great story to tell. We have conquered such dread diseases as yellow fever, cholera, the plague and smallpox. The occurrence of diptheria, scarlet fever, typhoid fever, and rickets, the latter a disease at one time so prevalent in the south, are indeed rare.

As recently as ten years ago, Rocky Mountain Spotted Fever killed as many as fifty per cent of those who were bitten by an infected tick and contracted the disease. Today, this deadly infection can be quickly cured with a few broad spectrum antibiotic capsules. The devastating consequences of syphilis and gonorrhea are now preventable and disappearing, thanks to penicillin and other antibiotics. A patient with these diseases can now be rendered noninfectious in a matter of hours and cured in a few days or weeks with drugs now being made available by pharmacy.

Our second greatest killer of fifty years ago—lobar pneumonia—which alone was responsible for 152 deaths per 100,000 population has now been so affected by the new drugs that the rate has declined to 12 per 100,000. Similarly, deaths from tuberculosis are now 22, where as in 1900 they were 195 per 100,000 and with the strides made in the treatment of tuberculosis today we even hope to reduce this rate materially. Forty years ago *one* of every *four* patients subjected to a major operation died, whereas today only 1 in 100 succumbs and this includes all patients young and old. We can cite many other examples which would equally show how, through the combined efforts of pharmacy and medicine, many of the diseases of the good old days have virtually been eliminated. Unlike the price of butter, eggs and coffee, the quality and quantity of medical care today are much better than they were back in the good old days.

Today the American Public is living longer thanks to our health professions. A child born in 1900 could hope to live about 44 years. Today the average life expectancy of each of the over 4 million babies born in 1953 is almost 70 years, or over 20 years of useful life, per baby, added to the productive resources of our country in a short span of 50 years. Even the dread disease polio has responded to pharmaceutical and medical research and there is now hope that the present vaccine or other vaccines will soon be developed, which will greatly reduce the incidence and hazards of this dread disease.

What about the costs of these services? Medical costs are not high . . . the public and pharmacists think they are. . . . What appears to be expensive is the vastly improved care and comfort

which is taken for granted by even the poorest of us, but 20 years ago was not available to the wealthiest. Since sickness is a condition which none of us request and usually none of us made adjustments for in our budgets, complaints will frequently arise. However, it is the responsibility of each one of us to answer these complaints, no matter which phase of the profession we might be in. Not to answer them with vague or unacceptable explanations, but to answer them with true basic facts.

Let us look at some interesting figures. In 1929, the American Public spent slightly over 3½ billion dollars for medical care or approximately 4.1% of the income of the country. In 1951, the total medical care bill was about 9 billion or approximately 4.3% of the national income. In 1929, physicians received 31.8 cents of each medical care dollar spent. Today they only receive 28 cents. In 1929, out of each medical care dollar 19.5 cents went for drugs and sundry items, today only 17 cents of the medical care dollar goes toward paying for drugs and sundry items.

Yet we are continually told drug costs are high and we believe it. Let's look at some other interesting figures. In 1952, according to the U. S. Department of Commerce, each person in the United States spent the following amounts for various services and commodities:

Alcoholic Beverages	$55.
Tobacco Products	$32.
Auto Repairs and Maintenance	$11.
Amusements	$10.
Drugs and Sundries	$10.

Is our alcohol more important than our bodies?

What can you as individual pharmacists do you might ask? It is upon you that the whole problem rests. You are the link with the public and it is you who must serve as a foundation for improved public relations. The public is interested in Health today and the cost of medical care has been exaggerated into a problem which has succeeded in instilling an element of question in the minds of a number of people. This extreme interest in Public Health is being somewhat exploited by a number of newspapers and magazines. We as a profession must constantly be alert to make certain that the public are apprised of the true facts on our contributions. As I witness the facts, we must first rid ourselves of this inferior and lethargic attitude so prevalent in our ranks. We must put our best foot forward and

have our stores and ourselves assume an air of professional dignity. The public will not think any more of us than we think of ourselves.

One additional subject which many of us overlook as having to do with public relations is the economic side of pharmacy. You may rightfully ask, "What does economics have to do with Public Relations?" There are two sides to the practice of pharmacy—the scientific side and the business side. Being proficient in each is extremely important. Poor business practices are frequently at the bottom of patients' complaints about medical care and its practitioners. Your own financial well-being is closely tied in with your ability to create good public relations. Financial pressures will undermine pharmacy's ability to provide excellent pharmaceutical service and thus adversely affect our public relations.

Remember that efficiency in economic matters is to the best interest of both you and your patient. You will serve your patients effectively and efficiently by running your business correctly and making a realistic modest profit. It is unquestionably wrong to overcharge for services, but it is equally as wrong and dangerous to charge too little. The fair price is best. Most people aren't looking for bargains in medicine. The average person is willing to pay a fair price for good pharmaceutical service and a fair price must be one which is equally fair to the patient and to yourself.

We have a most interesting story to tell and we must get out and tell it. It is a dramatic and dynamic story; one continually changing. When we stop to realize that 60 per cent of the prescriptions being compounded today were unknown 5 years ago while over 80 per cent were unknown 10 years ago, we see how dynamic a profession it is; and this search for progress has not stopped. It is estimated that in 1954, well over 250 million dollars will be spent for medical research in this country. More progress must be made.

Thus, I trust that I have left with you the fact that Public Relations is everyone's job, yours and mine, the wholesaler, the teacher, the manufacturer, the hospital pharmacist, the organizations, but more important the individual retailers. The road ahead is not easy; we have a story that needs telling and we must tell it. The value of the pharmacist's professional services and medication must be explained and proven beyond a doubt for the future of pharmacy is at stake. Accept the challenge as individual pharmacists, for you have a most important stake in that future. Remember—"The only person who can afford to be asleep at the switch is the man who sleeps *under* an electric blanket.

SELECTED ABSTRACTS

The Sterilization of Ascorbic Acid Solutions. Bryan, G., and D'Arcy, P. F. *Pharm. J. 172:247* (1954). The stability of ascorbic acid solutions during sterilization and subsequent storage was investigated by the authors. The means of sterilization employed were, filtration through bacteriological filters, heating in free-flowing steam for 30 minutes, or autoclaving at 115° C. for 30 minutes. The following formula was that of the starting solution:

Ascorbic Acid	5.0	Gm.
Sodium Bicarbonate	2.38	Gm.
Thiourea	0.012	Gm.
Water for Injection q.s.a.d.	100.000	mls.

The pH of this solution was about 6.4.

Samples of the solution were assayed before and immediately after the sterilization treatment. The steamed solutions showed a loss of 1.43 and the autoclaved solutions a loss of 3.1 per cent of potency. In order to consider the steaming a sterilization process, the bacteriostatic agent, 0.2 per cent chlorocresol, was added to the formula. When the antioxidant, thiourea, was omitted from the formula the loss of potency was approximately doubled. However, there was no appreciable further loss of potency upon storage for up to 9 months.

The effect of pH on the stability of the solutions was also investigated. It was found that sodium bicarbonate and ascorbic acid formed an effective buffer at pH 6.8. Sodium hydroxide was, therefore, used to obtain higher pH values. Solutions were adjusted to pH values between 2.5 and 8.1 and then filtered or steamed. Using the filtered solution as the control the loss in potency of the steamed solution was determined. The most stable solution had a pH of 5.6 but the solution with a pH of 6.4 had only a slightly higher loss, 0.46 and 0.70, respectively.

The authors, therefore, concluded that sterilization by filtration or by steaming with a bacteriostatic agent produces essentially the same loss of potency, which is not further increased significantly during storage for 9 to 12 months, provided an antioxidant is present and the pH of the solution is not higher than 6.4.

Oral Electrolyte and Phthalylsulfacetamide Therapy in Diarrhea. Stephens, L. J., and Henrickson, W. E. *Missouri Med. 51:*283 (1954). The importance of the oral replacement of electrolytes in the treatment of the early stages of diarrhea in infants and small children was emphasized by the authors in their report of 166 cases of mild to severe diarrhea. In 75 of the cases a regimen of treatment was adopted which provided for electrolyte replacement as well as chemotherapeutic therapy of the intestinal tract. A solution containing 10 Gm. of sodium and potassium lactate (representing 0.8 Gm. elemental sodium and 2.5 Gm. elemental potassium), 4 Gm. phthalylsulfacetamide, 4 Gm. sodium carboxymethylcellulose, and 5 Gm. glucose in each 100 cc. was given orally in divided doses in the amount of 5 cc. per Kg. of body weight in each 24 hours. This was the usual dose, but in the more severe cases as much as twice this amount was given. The solution was diluted with water for administration.

This treatment resulted in a shortening of the duration of the symptoms of the diarrhea. The authors concluded that the treatment was effective in 89 per cent of the cases.

The Long-Term Administration of Antibiotics in Chronic Bronchopulmonary Suppuration. Finke, Walter. *Antibiot. and Chemother. 4:*319 (1954). A seven year study of the rationale of long-term antibiotic therapy of chronic bronchopulmonary suppuration as manifested in chronic bronchitis, infectious asthma, and pneumonia was investigated by the author. A series of 244 patients were treated and/or followed for over a year with an average of 2.75 years.

Penicillin was the mainstay of therapy. As the study progressed, parenteral therapy was more and more replaced with aerosol and oral therapy. Dosage was also reduced to from 500,000 to 1,000,000 units daily by mouth or 200,000 to 500,000 units by aerosol 1 to 3 times a day. Other antibiotics were combined in many cases. Streptomycin or dihydrostreptomycin was given parenterally or by aerosol in doses rarely exceeding 0.5 Gm. a day. Chlortetracycline, oxytetracycline and chloramphenicol were given orally in doses of less than 1 Gm. a day. During the early portion of the study, large doses orally of the broad spectrum antibiotics and large parenteral doses of penicillin caused serious complications in some cases. However,

by limiting the use of parenteral penicillin, by avoiding large doses of the other antibiotics, and by close observation of all treated patients, complications from therapy were largely eliminated.

The long-term therapy gradually reduced the number of exacerbations of the infections. Of the 135 adults in the study only 1 developed pneumonia and 2 status asthmaticus during a particular year. An incidence of about 15 per cent occurred in a control group. Similarly, a sharp decrease in the incidence of pneumonia was seen in the 109 children in the study as compared with a control group. Acquired resistance did not appear as a clinically appreciable phenomenon in this study. The author concluded that long-term antibiotic therapy can cure early cases and rehabilitate advanced cases of chronic bronchitis and infectious asthma and that patients afflicted with such conditions face a smaller health risk from this therapy than from certain of the symptomatic remedies.

Intramuscular Administration of Oxytetracycline. Montmorency, F. A., Caffery, E. L., and Musselman, M. M. *Antibiot. and Chemother. 4*:313 (1954). A satisfactory formula for the intramuscular administration of oxytetracycline solutions was investigated by the authors. Four different formulations were tried, the composition of which follows:

	No. 1	No. 2	No. 3	No. 4
Oxytetracycline hydrochloride	123.3 mg.	——	100 mg.	100 mg.
Oxytetracycline base	——	100 mg.	——	——
Sodium glycinate	111.0 mg.	——	——	——
Polyvinylpyrollidone	111.0 mg.	——	——	——
Sodium bisulfite	7.1 mg.	——	——	——
Procaine hydrochloride	55.5 mg.	15 mg.	15 mg.	20 mg.
Magnesium chloride anhydrous	——	25 mg.	25 mg.	——
Magnesium chloride hexahydrate	——	——	——	100 mg.

A total of 1880 intramuscular injections were given in doses of from 50 to 250 mg. to 313 individuals. Single doses of 100 mg. or more provided adequate blood levels with all four preparations. How-

ever, an increase in the dose above 100 mg. did not proportionately increase the blood level. When a dosage of 100 mg. was repeated every six hours a blood level of 1.5 μg. or more was attained in all cases.

The formulas as given were dissolved in Water for Injection to give a concentration of from 50 to 100 mg. per ml. In most cases the volume of solution injected was 1 ml. Formulas 1 and 2 produced severe pain when injected, along with tenderness and induration which lasted from 48 to 72 hours. With formulas 3 and 4 there was little or no pain and virtually no tissue reaction. A dosage of 250 mg. of formula 4 in a volume of 2.5 ml. was well tolerated at intervals of 12 hours for 5 days. The addition of 500 units of hyaluronidase to formula 4 did not conclusively alter the blood levels of the antibiotic and the discomfort or tissue reaction was not altered.

The authors concluded that formulas 3 or 4 should be clinically satisfactory for the intramuscular administration of oxytetracycline hydrochloride in a concentration of up to 100 mg. per ml.

Symposium on the Management of Complications of Antibiotic Therapy. Nelson, C. T., Lattimer, J. K., Barach, A. L., and Flood C. A. *Bull. N. Y. Acad. Med. 30:*540 (1954). Nelson discussed the various types of dermatologic complications of antibiotic therapy. He pointed out that the urticarial or serum sickness type of reaction could best be treated with the antihistamines in relatively large doses. In other types of untoward dermatologic reactions, such as maculo-papular eruptions, the eczematoid responses, mucous membrane manifestations, and contact dermatitis, the antihistamines are of little value. For the severe types of dermatologic manifestations the corticosteroids are indicated. Although the dosages required are high, for example, cortisone 300 mg. daily for 3 days then reduced by daily decrements of 50 mg., there is little danger from their use since the period of administration is usually quite brief. In the local care of the skin, if the eruption is merely morbilliform, a bland emollient such as Calamine Liniment N. F. may be used. Where there is weeping or oozing, wet compresses of aluminum acetate solution 5 per cent diluted 1:50 or normal saline may be used. In cases of stomatitis, warm saline mouth washes are satisfactory and in the case of vaginitis or perianal dermatitis, douches or wet compresses of silver

nitrate solution 1:5000 are helpful. The most important management approach in all of these reactions is to stop the administration of the antibiotic.

Genito-urinary complications were discussed by Lattimer. Monilial vaginitis is a complication occurring rather frequently, particularly in women past the menopause. The treatment recommended was saline irrigations for a day or two followed by dilute solutions of silver nitrate, and then a 1 per cent solution of gentian violet. Crystalluria due to sulfonamides was mentioned, particularly resulting from the use of sulfadiazine. Alkalizing adjuvants and forcing of fluids are essential means for the management of the condition. Drug resistance occurs with increasing frequency. Such a problem can best be managed by determining the drug to which the organism is sensitive and then administering sufficiently large doses to effect a cure, at the moment most appropriate for therapy. Another complication sometimes seen is a cholera-like toxemia resulting from an over-growth of a resistant staphylococcus during therapy to sterilize the bowel. The proper approach in such cases is to head off the over-growth by making culture studies of the bowel contents. A final complication discussed by Lattimer was toxicity directly due to the chemotherapeutic agent, particularly with reference to the therapy of tuberculosis where the drugs are given over a long period of time. The ataxia and deafness formerly commonly seen with streptomycin therapy has been reduced by giving the drugs less frequently and by combining both streptomycin and dihydrostreptomycin. Drug resistance to streptomycin PAS and isoniazid is reduced by always giving combined therapy rather than one agent alone.

The allergenic reactions to antibiotic therapy can be managed in a number of ways, but the complications may be serious. In fact, Barach suggested that the time may have come to limit the use of intravenous pencillin to those conditions in which exceptionally high blood levels of the antibiotic are required for survival. Probably the most serious allergenic reaction is anaphylactic shock. Artificial respiration, oxygen therapy, and intravenous antihistamines and adrenalin may be necessary. The author pointed out that the bronchospasm sometimes encountered with aerosol therapy of penicillin is probably due to the impact of the mist and not to an allergenic reaction. He also discussed the development of bacterial resistance and the secondary infections occurring from resistant organisms.

Flood discussed the gastrointestinal complications of antibiotic therapy. These are usually not serious and include nausea, vomiting, diarrhea, and pruritis ani. They chiefly occur following the administration of the broad spectrum antibiotics. Fortunately, a glass of milk given along with each dose of the antibiotic will usually control the nausea. The more serious complications of diarrhea, and ulceration of the lower intestinal tract do not occur frequently. When they do occur, the present theory of the cause—a disturbance of the intestinal flora causing vitamin B complex deficiency and moniliasis, forms the basis for therapeutic management.

The Rectal Administration of Urethane in Leukemia. Suhrland, L. G., and Weisberger, A. S. *J. A. M. A. 154:*1415 (1954). The effectiveness of urethane in the relief of the pain in plasmacytic leukemia and in the treatment of chronic granulocytic leukemia has been established. However, the usefulness of this drug in these conditions has been considerably limited by the marked side effects which develop in about half of the patients under treatment. These side effects consist of anorexia, nausea, vomiting, and diarrhea. In many cases they are so severe that therapy with urethane must be discontinued.

Therefore, the authors investigated the possibility of rectal administration of the drug. Suppositories composed of a base of beeswax and theobroma oil and containing 1 Gm. of urethane each were given to 20 patients. The daily dosage varied from 3 to 6 Gm. and was continued for from 2 weeks to 22 months.

It was found that urethane was effectively absorbed through the rectum. This conclusion was based on the fact that it was as effective as Fowler's solution in spacing irradiation therapy in chronic granulocytic leukemia. Based upon leukocyte counts and subjective improvement, the authors found that rectal therapy was as effective as oral therapy in both of these types of leukemia. In addition, the side effects were minimal. One patient among the 20 patients treated complained of mild nausea while receiving 6 Gm. of urethane a day by rectum. Another patient developed diarrhea which required discontinuation of treatment. No other gastrointestinal symptoms were observed and there was no evidence of rectal irritation.

The authors concluded, therefore, that the rectal administration of urethane is preferable to oral administration.

BOOK REVIEWS

The Symptoms and Treatment of Acute Poisoning. By G. H. W. Lucas; 308 pages incl. index. The Macmillan Company, New York, 1953.

This book represents a concise treatise on the therapy of poisonings. It is published in octavo form and is thus suitable to be carried in the pocket. The first chapters deal with general principles of the treatment of poisonings. Special consideration is given to poisoning in children. The chapters entitled, "Suggested Supplies and Apparatus" (for the treatment of poisonings) and "Some Useful Drugs and Preparations", contain helpful advice for physicians and hospital pharmacists for the setting up of toxicology units. A brief chapter deals with "Collection and Preservation of Samples for the Analyst". In the subsequent chapters, the most important medicinal, industrial, food, and animal poisons are discussed alphabetically.

It is a matter of opinion which poisons should be included in a small volume. The reviewer missed the inclusion of sodium fluoroacetate, DFP, OMPA, and a number of war gases.

The nature, main applications, symptoms, and treatment of poisoning are discussed in each section. A table of fatal doses is a particularly useful addition. Few toxicology texts contain the latter, especially in such thorough revision.

JULIAN L. AMBRUS

The Pharmacologic Principles of Medical Practice, Third Edition. By J. C. Krantz, Jr. and C. J. Carr; 1183 pages incl. index. Williams & Wilkins Co., Baltimore, 1954.

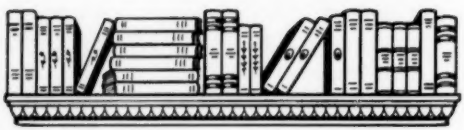
This textbook is intended primarily for medical students and physicians but it is also very well suited for pharmacy students and as a reference book for pharmacists.

In preparing the third edition, the authors have made changes in keeping with the many recent advances made in medicine and medicinals. It is arranged in nine parts each covering a broad field; each in turn is subdivided into numerous chapters dealing with a group of related drugs.

This reviewer feels that the authors have tried and succeeded in making the book a useful compromise on basic pharmacology and practical therapeutics. Some texts which are devoted only to fundamentals of pharmacology with their contradictions leave the student so confused that it is small wonder that he either learns medicine from detail men or becomes a therapeutic nihilist. The student using this text can obtain a useful working knowledge.

A random check of various recent data gave evidence that the authors have reviewed the literature well in preparing this new edition. It should be well received.

L. F. Tice



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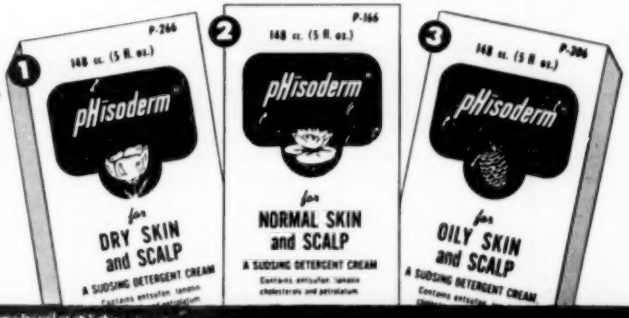

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American Journal of Pharmacy

The American Journal of Pharmacy is the oldest continuously published scientific periodical of its kind in America, having been established by the Philadelphia College of Pharmacy in 1825. After the original issue there were three other preliminary numbers until 1829, when regular publication began. From then until 1852 four issues were published annually, with the single exception of 1847, when an additional number appeared. Six issues a year were printed from 1853 to 1870, at which time the Journal became a monthly publication.

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